NON-TECHNICAL ABSTRACT

This research is being done to evaluate an approach that uses the transfer of a gene (referred to as "gene therapy") as a method to treat patients with locally advanced (unresectable) pancreatic cancer. The gene therapy approach in this study uses adenoviruses (AdV) from which scientists have removed pieces (viral genes) so they cannot replicate (make more viruses) efficiently outside of the laboratory. These replication-deficient viruses are called vectors, and are used as vehicles to transfer genes into cells. Normal adenoviruses that have all their genes and do replicate efficiently are common in humans and generally cause mild infections and colds. A herpes virus gene called *thymidine kinase* (tk) was inserted into the adenoviral vector. The resulting vector is called AdV-tk. The AdV-tk vector is injected into the tumor leading to production of the TK protein in infected tumor cells. The TK protein is what makes cells infected with herpes virus susceptible to anti-herpes drugs like valacyclovir. Valacyclovir is a Food and Drug Administration (FDA) approved drug for treating herpes infections and results in the death of cells containing the TK protein. After the AdV-tk injection into the tumor, subjects will be given valacyclovir pills for 14 days.

Standard treatment for unresectable pancreatic cancer consists of chemotherapy and radiation (chemoradiation). Studies in laboratory animals suggest that the addition of AdV-tk gene therapy to chemotherapy and radiation therapy may be beneficial.

The main purpose of this study is to evaluate the safety of this gene therapy approach in people with pancreatic cancer receiving standard chemotherapy and radiation therapy. Based on previous experience with this gene therapy approach for other types of cancer, we do not expect significant side effects. However, since this approach has not been used in people with pancreatic cancer, we will first evaluate escalating doses of AdV-tk to determine if the doses we propose can be given without causing severe or unmanageable side effects. Once a safe dose level has been determined, we will proceed with the Phase II part of this study to further evaluate safety in more people at that dose level and assess whether the approach appears effective at fighting pancreatic cancer.